ETIOLOGY, OUTCOME AND RISK FACTORS FOR EMPYEMA THORACIS IN CHILDREN AGED 1 MONTH – 12 YEARS IN A TERTIARY CARE CENTRE

Dissertation submitted for

M.D. DEGREE EXAMINATION
BRANCH VII- PAEDIATRIC MEDICINE

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY
CHENNAI

APRIL 2013

INSTITUTE OF CHILD HEALTH AND HOSPITAL FOR CHILDREN
MADRAS MEDICAL COLLEGE
CHENNAI

CERTIFICATE

This is to certify that the dissertation titled **"ETIOLOGY, OUTCOME AND RISK FACTORS FOR COMPLICATION OF EMPYEMA THORACIS IN CHILDREN AGED 1 MONTH – 12 YEARS IN A TERTIARY CARE CENTRE"** submitted by **Dr. ARUNAGIRINATHAN.V.,** to the Faculty of Pediatrics, The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of M.D. Degree (Pediatrics) is a bonafide research work carried out by him under our direct supervision and guidance.

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DECLARATION

I **Dr.ARUNAGIRINATHAN . V.,** solemnly declare that the dissertation titled **"ETIOLOGY, OUTCOME AND RISK FACTORS FOR COMPLICATION OF EMPYEMA THORACIS IN CHILDREN AGED 1 MONTH – 12 YEARS IN A TERTIARY CARE CENTRE"** has been prepared by me.

This is submitted to the **Tamilnadu Dr. M. G. R. Medical University**, Chennai in partial fulfillment of the rules and regulations for the M.D.Degree Examination in Paediatrics.

Dr.ARUNAGIRINATHAN.V.

Place : Chennai

Date :

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CERTIFICATE OF APPROVAL

To
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Dear Dr. V. Arunagirinathan

The Institutional Ethics Committee of Madras Medical College reviewed and discussed your application for approval of the proposal entitled " Etiology, outcome & Risk factors for complications of empyema thoracis in children aged 1 month -12 years in a tertiary centre " No. 11102011.

The following members of Ethics Committee were present in the meeting held on 20.10.2011 conducted at Madras Medical College, Chennai -3.

1.	Prof. S.K. Rajan, MD	-- Chairperson
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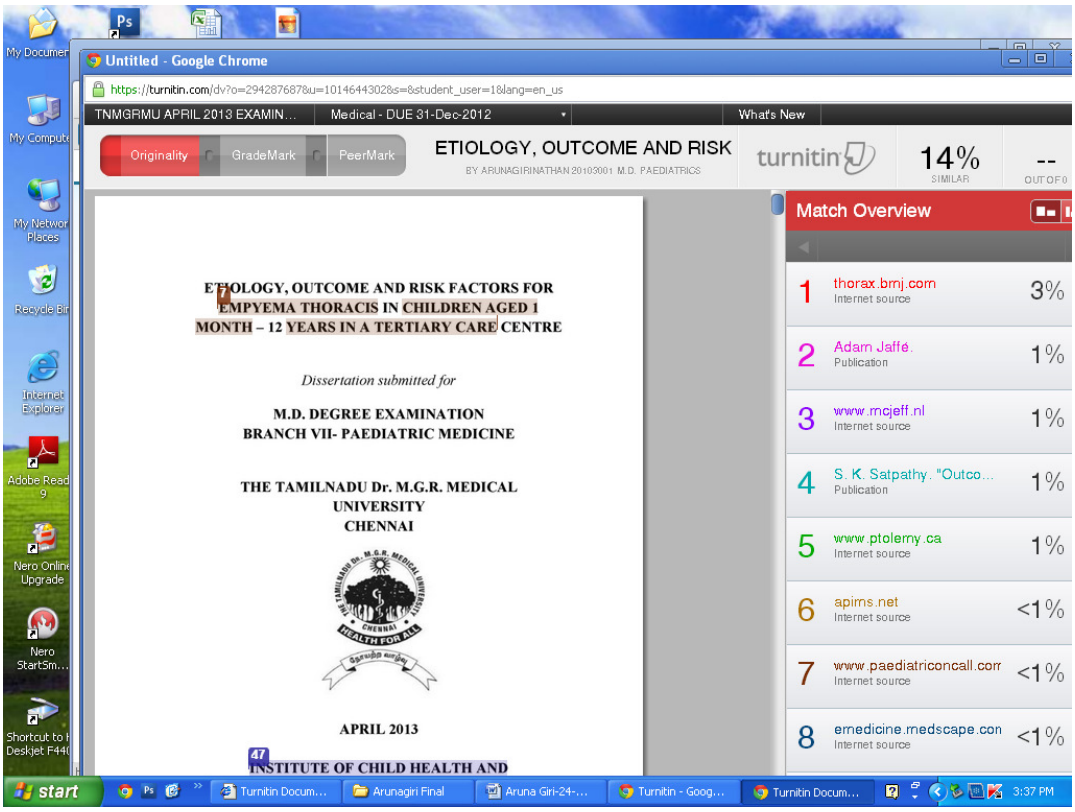
7.	Tmt. Arnold Soulina MA	-- Social Scientist
8.	Prof. Shanta Ravishankar Prof of Neuropathology, M M C, Chennai -3	-- Member

We approve the proposal to be conducted in its presented form

Sd /. Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information / informed consent and asks to be provided a copy of the final report

Member Secretary, Ethics Committee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INTRODUCTION

Empyema thoracis is recognized as one of the serious complications of pneumonia for centuries. Hippocrates in 500 Bc gave the first description of parapneumonic effusion and recommended open drainage as treatment modality. Thoracentesis as treatment option for Empyema thoracis was introduced by Trousseau in France and Bowditch in USA (4). Hewitt then used a rubber tube with a cannula inside to place it inside the cavity. He was the first person to use water seal drainage for Empyema thoracis. Next advance in the treatment option of Empyema thoracis was thoracoplasty which involves resection of ribs; inter costal muscles and thick pleural peal. The remaining defect was covered with muscles, scapula, subcutaneous tissue and skin (4).

Decortication as a treatment option was first reported by Eggers in 1923(4). Enzymatic debridement using a combination of streptokinase and streptodornase was used by Tillet and Sherry for treating parapneumonic empyema (4). In 1972 Light came out with an important observation that low pleural fluid pH was associated with loculated effusion and an indicator for tube thoracostomy (4). He also

came with Light's criteria for differentiating pleural fluid as transudate and exudate. The latest development in empyema thoracis management was invention of Video Assisted Thoracoscopic Surgery (VATS).

Definitions

Parapneumonic effusion is defined as any pleural effusion which is associated with pneumonia, bronchiectasis or lung abscess.

Empyema is defined as pus in the pleural space.

Evolution of pleural infection is a continuous process which is divided into three different stages which are not very sharply delineated

a. **Exudative** – The stages marked by out pouring of sterile pleural fluid into the pleural space secondary to inflammatory changes associated with underlying pneumonia. Pleural fluid white blood cell count, LDH, glucose level and pH are normal. Initiation of appropriate antibiotic at this stage can avert the need for tube thoracostomy.

b. **Fibropurulent stage** – This stage is marked by deposition of fibrin in the pleural space with accumulation of pleural fluid, leukocytes , bacteria and cellular debris. This in turn leads to formation of loculation and septation. Both complicated parapneumonic effusion and simple Empyema come under this stage.

c. **Organization stage** – Fibroblast grow into the exudates from both the visceral and parietal pleura leading to the formation of pleural peel or pleural rind. This pleural peel may prevent lung re-expansion leading to trapped lung. This empyema cavity is a potential source of infection leading to complications like bronchopleural fistula, septicemia, etc.

Epidemiology

Incidence of parapneumonic effusion and Empyema was found to be 3.3 per one lakh children (1). Annual incidence of bacterial pneumonia estimated to be 4 million and 25% of this requires hospitalization and of this 40% have pleural effusion (11). Empyema occurs in 5% to 10% of bacterial pneumonia and up to 86% children with necrotizing pneumonia (2). Parapneumonic effusion and Empyema are more commonly found in boys and are encountered

more commonly in children less than 2 years. They commonly occur in winter and spring (1).

Pathophysiology

Normally pleural space contains 0.1 to 0.2 ml/kg of sterile colourless fluid. The pleural fluid circulation is balanced by secretion and absorption of fluid by lymphatic drainage (stoma of parietal pleura).When this homeostasis is altered by infection, inflammation, malignancy - pleural fluid will accumulate in the pleural space. Infection leads to pleural inflammation which in turn increases permeability and influx of bacteria and inflammatory cells such as neutrophils. This inflammatory cascade is further amplified by cytokine release from mesothelial cells (4). Activation of coagulation cascade leads to decreased fibrinolysis and deposition of fibrin which causes classical features of loculation, septation and peel formation in later stages of Empyema.

Microbiology

The rate of identification of any organism from pleural fluid varies between 8 and 76 %(5). Definite data regarding the incidence of various organisms is missing because of various factors like

differences in the incidence, inclusion and exclusion criteria, different pleural fluid sampling rate and different culture methods. Further, prior usage of antibiotics also hampers the yield of pleural fluid culture results. Even with modern cadgets like pneumococcal or16S PCR yield of positive results is around 75% of culture negative cases. Streptococcus pneumoniae followed by Streptococcus pyogenes and Staphylococcus aureus were most common organisms cultured during pre -antibiotic era. With advent of antibiotics the proportion of staphylococcus aureus increased (5). At present streptococcus pneumoniae is predominant organism in the developed countries and staphylococcus aureus is the most common pathogen in developing countries (1). Even though pneumococcal pneumonia presents with effusions in 40% of the patients, empyema occurs only in 5%.Further the prevalence of pneumococci and Haemophilus has reduced since the introduction of vaccines (20). The causative organism in the order of occurrence is shown below,

Anaerobes are usually common in mixed infections and most commonly occurs secondary to aspiration pneumonia followed by lung abscess and spread from adjacent sites. Mycoplasma, Legionella and viruses can cause empyema very rarely. Mycobacterium tuberculosis is

responsible for about 6% of all cases worldwide (5). Fungal infection is usually hospital acquired and usually occurs in immunocompromised host.

Table 1 .Common Organisms causing empyema thoracis in children

Aerobic organisms	Anaerobic organisms
Staphylococcus aureus	Bacteroides species
Streptococcus pneumonia	Fusobacterium species
Haemophilus influenza type b	Clostridium species
Pseudomonas aeruginosa	Peptococcus
E.coli	Peptostreptococcus
Streptococcus viridians	Catalase negative non sporeforming G+ bacilli
Enterobacter species	Propionobacterium acne.
Legionella pneumophilla	
Mycobacterium tuberculosis.	

Predisposing factors

Factors that predispose to empyema are poor orodental hygiene, periorodental disease, cardiac diseases, prematurity, mental retardation, cerebral palsy ,immune suppression, neglected foreign body ,trauma and thoracic surgeries(3).

Child usually present with classical symptoms of pneumonia like fever, cough, breathlessness, effort intolerance, reduced appetite, night sweat, abdominal pain, halitosis and lethargy. Older children may complaint of a pleuritic chest pain and may prefer to lie on the affected side. Child on examination have decreased air entry on the affected side with reduction in vocal resonance and vocal fremitus and stony dull to percussion. Inter costal tenderness may be elicited sometimes. Persistence of fever spikes in a child with pneumonia started on antibiotics after 48 hours usually signifies the appearance of effusion (1). Fever may not be present in immune compromised and debilitated patients.

Investigation

A complete blood count may reveal anemia, increased or decreased total WBC count, and differential count with polymorph predominant. Blood urea, creatinine and electrolytes are done to detect abnormal renal function and inappropriate anti diuretic hormone secretion (SIADH). Blood samples are drawn and are send for culture and sensitivity. Acute phase reactants such as erythrocytes sedimentation rate (ESR), C - reactive protein (CRP) are unable to distinguish between viral and bacterial infection. However, similar to white cell count, CRP may be useful to assess progress in patients who remain febrile and are slower in recovery. Total serum proteins and serum albumin are usually low in cases of complicated empyema.

Addition diagnostic studies like tuberculin testing are done if tuberculosis etiology is suspected. Since 1/3 of tuberculous effusion may be mantoux negative two samples of early morning resting gastric juice aspiration are done and send for acid fast bacilli analysis. Purulent sputum that grow single predominant organism can be helpful in predicting the etiology for empyema. Test specific for other collagen vascular diseases are done when this diagnosis are entertained.

Imaging

X-ray chest AP or PA view usually shows obscured costophrenic angle with fluid tracing the lateral and posterior chest wall. Sometimes x-ray may reveal underlying lung consolidation which is easily made out by x-ray taken at various positions such as lateral decubitus or cross table view (4). Presence of pleural fluid greater than 10 mm in lateral decubitus view is usually taken as indication for thoracentesis in older children or adolescents with larger collection (greater than 1000 ml) of free pleural fluid with mediastinum shifted to opposite side. With organization of the pleural fluid discrete pockets containing loculated pus could be seen. Presence of air fluid level signifies generations of air by gas forming organisms or due to communication with the bronchus producing bronchopleural fistula(5) .

Chest ultrasound can detect the presence of fluid, septations, loculation and gives idea about the underlying lung parenchyma. Ultrasonography is very useful in the case of white out lung in the chest x-ray (4). It can estimate the size of the effusion, and determine the echogenicity of the fluid, differentiates between free and loculated

fluid. It can demonstrate pleural thickening and can be used to guide chest tube insertion. They are superior to CT chest for viewing fibrinous septations (1).

CT –scan chest is not routinely needed in all empyema cases. There are few indications for CT chest they are

1. To locate a bronchopleural fistula.
2. To locate a non opaque foreign body.
3. Usefull when the whole hemithorax is opaque and to know about the underlying lung.
4. Sometimes it is asked preoperatively before planning surgery. Contrast enhanced CT – chest demonstrates both parietal and visceral pleura as split pleura sign (20).

Thoracentesis

Indications are :

a) Large amount of fluid in anatomically accessible site.

b) If microbial diagnosis is intended.

c) Compromised pulmonary function.

d) To decide whether further intervention is needed.

e) If imaging does not show any evidence of organization.

Light and colleagues came out with criteria for diagnosing Exudative effusion they are :

1. Pleural fluid pH less than 7.2.
2. Pleural fluid protein to serum total proteins ratio greater than 0.5.
3. Pleural fluid LDH to serum LDH greater than 0.6.
4. Pleural fluid glucose concentration less than 50 mg/dl.

Any of the above criteria denotes Exudative pleural effusion. (32).

A pleural fluid cholesterol concentration greater 60 mg/dL can be used as extra diagnostic tool in patients with congestive cardiac failure who may have falsely elevated levels of pleural fluid proteins secondary to diuretic therapy. (32)

Gram stain of the pleural fluid is used for initial selection of empirical antibiotic therapy before culture and sensitivity becomes available. Total WBC count in empyema fluid may vary from 5000 – 50000 cells/cu mm and almost all cells are neutrophils in bacterial infection. Numerous small lymphocytes usually suggest tuberculous etiology and sometimes may indicate malignancy. Parasitic, fungal and sometimes tuberculosis may have marked eosnophilia in the pleural fluid. Specific stains are used for tuberculosis (ziehl –Neelsen staining, Auramine staining) and fungus (Potassium hydroxide mount).pleural fluid cytology is done when malignancy or metastasis is suspected. Pleural fluid amylase is elevated in esophageal rupture, acute hemorrhagic peritonitis, or pulmonary infarction. Recently various antigen detection systems are available for identification of pneumococcus and H.influenza type-b. PCR technique using 16Srna for pneumococcus and Mec – 300 gene probe for identifying

methicillin resistant staphylococcus aureus are used to identify organisms in culture negative cases(1)

Treatment

ACCP and the BTS came out with guidelines for the management of empyema thoracis. Although there are differences in management in both guidelines both recommend that the pleural space should be drained in all patients with exudative PPE with pleural fluid pH < 7.2 and in those who have frank pus in the pleural space. Both recommend the usage of antibiotics in all patients with parapneumonic effusion in addition to the primary treatment of either VATS or tube thoracostomy (4).

Conservative management of empyema thoracis include:

i. Suplemental Oxygen if necessary (saturation less than 92%)
ii. Fluid therapy with isotonic fluids can be started if the child is dehydrated or unable to drink
iii. Initiate intravenous antibiotics alone or
iv. Antibiotics with chest tube drainage.
v. Analgesia and antipyretics
vi. Physiotherapy is not indicated.

All patients with Empyema thoracis are started on IV antibiotics and conservative treatment is either antibiotic alone or antibiotic with chest tube drainage. Chest tube drainage is always useful because it reduces the septic load. Any enlarging effusion which compromises respiratory function should be drained by tube thoracostomy. There is no role of repeated thoracentesis in treating empyema and if repeated tapping is expected chest tube should be inserted at the first time itself. Choice of antibiotics is in accordance with the BTS guidelines for community acquired pneumonia. Empirical treatment must cover Streptococcus pyogenes, Pneumococcus and Staphylococcus aureus. It is prudent to add anti staphylococcal antibiotics when evidence of skin infections or pneumatocele in chest x ray is present.

Coverage for anaerobes should be initiated in children prone for aspiration for example, developmental delay, cerebral palsy, mental retardation, seizure disorder etc. The various antibiotics options are;

1. Cefuroxime
2. Amoxycillin with clavulanic acid
3. Amoxycillin and flucloxacillin
4. Penicillin and flucloxacillin
5. Clindamycin

If aspiration is suspected metronidazole may be added in older children. Broad spectrum antibiotic covering Gram positive, Gram negative and anaerobes should started in hospital acquired pneumonia. Empirical antitubercular treatment is usually not started until there is definite evidence of tuberculosis. Whenever possible antibiotic course must be guided by the culture sensitivity reports. Since the pleural fluid cultures are usually negative antibiotics are continued based on clinical response. Oral antibiotics like amoxicillin with clavulanic acid are continued for 1-4 weeks after discharge. In patients from areas with high incidence of MRSA who are not severely affected may be started on clindamycin and for severely affected children vancomycin may be added. In patients at risk of acquiring gram negative organisms (neonates, post surgical patients) addition of aminoglycosides or a third or fourth generation cephalosporin may be useful.

Chest tube drainage

It was found that larger drain does not offer any added advantage than smaller drains in the management of empyema thoracis. Various studies have shown that small drains are effective and children are able to move more freely with small drains which in

turn accelerate recovery. Chest tube is usually inserted with sonography guidance at optimum site to drain fluid. Larger drains are usually inserted in the safe triangle, which is bounded by anterior border of latissmus dorssi and lateral border of pectorlis major muscle and a line drawn superior to the level of nipple and apex below the axilla. Substantial force should never be exerted while inserting a tube because sudden penetration of the chest may injure vital structures. Tube should be immediately connected to water seal drainage and it should always be kept at a level below the chest. The tube should be clamped for one hour for every 10 ml / kg of fluid evacuated to prevent re expansion pulmonary edema. Chest tube insertion should always be followed chest x ray to check out for adequate tube placement. Amount of pus draining every day should be noted and if there is no drainage, tube patency should be checked by flushing the tube with normal saline .Decision to remove the tube is purely clinical and is based upon many factors like the amount of fluid draining, child wellbeing, temperature and ultrasound evidence of residual pleural fluid and fall in acute phase reactants. Older children can be asked to do Valsalva maneuver during removal of the tube. A chest x ray has to be repeated after chest tube removal to rule out any pneumothorax.

Fibrinolytic therapy

Fibrinolytic agents like streptokinase or urokinase are instilled into the pleural space. They promote pleural fluid drainage, reduces fever by decreasing the septic load and reduces the need for surgical intervention. Streptokinase is used in the dose of 15,000U/kg diluted in 50 ml of normal saline (0.9%) daily for three days. Urokinase is used in the dose of 40,000U/kg in 40 ml of saline every 12 hours for 6 doses. Adverse reactions include anaphylaxis in the case of streptokinase and both the drugs are associated with hemorrhage.

Surgical intervention

1. Main indications for surgical referral are,
2. Failure with conservative management.
3. Child having persistent sepsis in spite of seven days of antibiotics.
4. Complex empyema with multiple loculation and thick pleural rind formation.
5. Broncho pleural fistula with pyopneumothorax.
6. Anaerobic infection, Scoliosis and lung entrapment (1).

Various surgical options available are:

1. Video assisted thoracoscopic surgery- Here the pus in the pleural cavity is drained and adhesiolysis and debridement of the fibrinous pleural material is done. It is a safe procedure with less pain and reduced hospital stay and leaves three small scars.
2. Mini Thorocotmy - Debridement of the fibrinous material with pus evacuation is done by an open procedure leaving a small thin linear scar.
3. Decortication - It is done through a formal posterolateral Thorocotmy incision with complete removal of the pleura rind with evacuation of the pyogenic material. It is a more invasive procedure leaving a long linear scar.

Supportive care

Fever is the common symptom in these patients and they must be adequately treated with paracetamol after checking temperature. Adequate analgesia is to be given during chest tube drainage and after surgical procedure.

Further it is recommended that these children are to be evaluated for immune dysfunction during the follow up period and also for cystic fibrosis by sweat chloride test.

Prognosis

This mainly depends upon the causative factor and the patients, who were previously well, recover without complications. The immediate mortality rate from empyema thoracis ranges between 0 – 10.8 %, and those with decortications ranges between 4 – 43 %. Patients who improved with conservative management ranges between 62- 80 %(20).

REVIEW OF LITERATURE

S.K.Satpathy, et al conducted a prospective study in the department of pediatrics and physiology M.K.C.G. Medical College Orissa, India from July 2001 to June 2003. Totally 53 cases of parapneumonic empyema was admitted in the hospital during the study period were included in the study .Neonates and other secondary cases of empyema thoracis were excluded from the study. Presence of frank pleural pus in the presence of organism with evidence of pneumonia or parapneumonic exudates with high polymorphs were taken as case definition. All cases except those presenting with multiple loculation were managed conservatively with chest tube drainage, intravenous antibiotics and supportive treatments. Thoracotomy surgery was performed in cases with multiple septations, failure with conservative management and bronchopleural fistula. They found that majority of cases (90.5%).9.4% in thoracotomy and 5.8% needed salvage thoracotomy following non improvement with chest tube. They concluded saying long term outcome of conservative management with chest tube drainage in parapneumonic empyema is comparable to primary surgical drainage (6).

Embiya Dilber, et al ,conducted a prospective study in the Department of pediatrics and physiology ,karadeniz University Faculty of Medicine Trabzon , Turkey from January from 2001 to June 2002.Totaly 38 consecutive patients were admitted for parapneumonic empyema in the age group of 6 months to 14 years were included in the study along with pleural fluid analysis quantitative assessment of C reactive protein and erythrocytes sedimentation rate were done on the day of admission and periodically repeated. Periodical white blood cell count was also determined. Plasma CRP levels were elevated in all patients and the mean time required for CRP to become normal was 16.4 days.ESR was also elevated initially and the mean required to reach the normal value was 27.6 days. The author conclude saying that serial determination of CRP proved useful in predicting complications and it is a sensitive marker not only for diagnosis but also for follow up of treatment outcomes(28).

Dass et al did a retrospective analysis of 160 children at Department of pediatrics, NEIGRIHMS, Meghalaya, India among the 160 cases, 150 cases were included and 10 cases excluded from the study (8 cases had tubercular empyema and 2 had significant comorbidity.Majority of the children were less than 5 years old and pus

culture was positive in 32%.Streptococcus pneumoniae was the predominant isolate followed by staphylococcus aureus and Klebsiella Pneumoniae. Clustering of cases was more found between April to July. Lung collapse (18%), Pleural thickening (16.7%), pericardial effusion (8%) and bronchopleural fistula (3.3%) were the complications occurred .Mortality was 3.3% and 14 cases underwent decortication surgery (9.3%).Author conclude the study saying that, leading cause of empyema thoracis was streptococcus pneumoniae and conservative management with antibiotics and intercostal underwater seal draining or early fibrinolytic therapy if indicated are effective modes of treatment (29).

Mohammed, et al did a prospective study at department of pediatric surgery at children's hospital Lahore from January 2001 – December 2004. Among 128 patients of empyema thoracis secondary to community acquired pneumonia(CAP) admitted during the study period . 14 cases secondary to causes other than CAP were excluded from the study. Mortality in this series was 2.3% compared to 2% with patients with simple community acquired pneumonia. They found more number of CAP patients above 5 years were more prone to develop empyema. Staphylococcus aureus was the most common

organism isolated from empyema thoracis. Recurrent respiratory tract infection predisposes the children to develop empyema thoracis (10).

Hillard, et al did a retrospective case review of 48 children's admitted with parapneumonic effusion or empyema in Bristol Royal Hospital for children between January 1998 and March 2001.Main aim of the study was to review the clinical presentation of empyema and to examine the effect of various treatment strategies on short term outcomes. Streptococcus pneumonia was the commonest organism isolated followed by staphylococcus aureus. They found that thrombocytosis was common in cases of empyema thoracis. Author concluded the study saying patients who had thoracotomy done recovered quickly than patients who have managed conservatively with chest tube drainage alone. Those children who were treated with fibrinolytic therapy also had favorable outcome (30).

Cemal Ozcelik, et al conducted a retrospective review of 515 children admitted during the period between 1990 and 2002 at Dicle university school of medicine at Turkey. All the children had empyema thoracis secondary to Pneumonia. Staphylococcus aureus was the most common organism isolated (20-38%). Cultures were negative in

37.86% of the children .Mortality was 1.55% with no post operative mortality .Complete and partial response were obtained in 58 patients who underwent Fibrinolytic therapy and 12 patients underwent decortications surgery. Author concluded saying intra pleural fibrinolytic treatment can be tried in all patients in stage II empyema with multiple loculations. They found that the mortality and morbidity rates were lower in patients undergoing decortication in the absence of underlying lung consolidation (15).

Prema Menon, et al from the department of pediatric surgery and pediatric pulmonology, PGI, Chandigarh, India conducted a prospective study with 125 children admitted with empyema thoracis stage III and underwent decortication were analyzed. Study period was between August 2005 to December 2009 and the follow up ranged from 3 months to 4 years .The study was done to highlight the delay in referral and the response to surgical intervention and follow up. There were no procedure – related or any delayed death reported. Malnutrition was present in most patients during admission (88% -less than 50th percentile for weight). Consolidation, cavitary necrosis and poor complaints were the three significant changes which affected morbidity .The duration of the disease was directly related to the

thickness of the pleural and injury to underlying lung. Prolonged recoveries with irreversible changes were associated with delayed referral. Author concludes saying that early surgical intervention with open surgical debridement gives good results and the prognosis depends on the lung status at the end of surgery (8).

Ashish Kumar Gupta, et al did a prospective study with 60 patients less than 12 years of age between January 2006 and October 2007 at department of pediartric surgery M.Y hospital and MGM Medical College, Indore, India. After a detailed clinical examination and investigations child having post-pneumonic or tuberculous empyema were treated with standard protocols .63.3%childrens of less than four years of age, and staphylococcus aureus was predominant organism cultured followed by Pneumococcus and gram negative bacilli. The author concludes saying tube thoracotomy should be the primary mode of treatment to reduce the septic load and thoracotomy with decortications is safe in experienced hands. Decortication is a valuable tool in developing countries were access to other treatment modalities like fibrinolytics and VATS are not available freely(21).

T Sang KY, et al did a retrospective review of all consecutive patients with complicated parapneumonic effusion and empyema thoracis admitted at United Christian hospital Hongkong January 2003 to June 2005. Main objective was to relate various factors like antibiotics used, usage of fibrinolytics, pulmonologist opinion with adverse outcome. Streptococcus milleri (19) was the predominant organism cultured followed by bacteroides and Klebsiella pneumonia. It was found that fibrinolytics worked well if instituted within 4 days of diagnosis. The study further emphasizes that adherence to standard international protocols in empyema thoracis management optimizes the outcome and inputs from pulmonologist are needed for better outcome. The organisms isolated from pleural fluid in this study differ markedly from organisms causing CAP. Discordant antibiotic usage was associated with worse outcome (7).

Ghritlaharey, et al did a study at a tertiary hospital in MP, India. It was a retrospective study of 46 children with empyema thoracis admitted between January 2010 – December 2010. Most of the children were between 1 – 5 years old and about 85% of the children received conservative management and about 15 % needed decortication.There were no mortality. The author concluded saying

that most of the cases can be managed by tube thoracotomy with antibiotics and those who fail on conservative management needs more aggressive management with surgery (31).

Karen D Schultz, et al did a retrospective chart review of 230 children admitted with empyema thoracis in a period of 10 years between 1993 – 2002 at Texas Children Hospital, Houston. Majority of the children were between 1 – 5 years of age. Only 32 % of the pleural fluids cultured were positive. On comparing data between 1999-2000 and 2001 – 2002, they found that the prevalence of streptococcus pneumoniae has reduced. Further there was reduction in the rate of empyema cases and Staphylococcus became the most common organism isolated from pleural culture and 78% of that was MRSA.The use of early VATS significantly reduce the hospital stay when compared to late VATS. The author conclude saying that there is a change in microbiological profile of empyema thoracis and this is probably due to the introduction of pneumococcal vaccine (34).

Sanaullah Tareen, et al conducted a prospective study in the department of Pulmonology,microbiology, Pakistan Institute of Medical Science Islamabad, Pakistan from august 2006 to march 2007.

Totally 42 patients who fulfilled the diagnostic criteria for empyema thoracis were included in the study out of which 34 were male and 8 were female. Pleural fluids collected in four different syringes from each patient were analyzed for mycobacterium tuberculosis culture, aerobic and facultative anaerobes strain and culture, anaerobic culture and fourth for chemical analysis. Patients with multiloculated pus on chest ultrasonography and CT – scan chest which needed surgical management were excluded from the study. Out of the 42 empyema fluid only eleven yielded bacterial growth on culture. The author concluded saying Gram-negative rods (26%) were the common cause of empyema and the lower yield on culture was probably due to prior use of antibiotics (33).

HYPOTHESIS

- What is the clinical, microbiological profile and outcome in empyema thoracis in children?

- What are the risk factors associated with complications /death?

OBJECTIVES

To study

- Etiological profile and outcome of empyema thoracis in children aged 1month -12 years and

- Various risk factors for complications

STUDY JUSTIFICATION

- Empyema thoracis continues to be one of the severe complications of pneumonia contributing to mortality and morbidity in the form poor lung expansion, trapped lung, scoliosis, and bronchopleural fistula and post operative complications.
- Analysis of freshly diagnosed cases of empyema thoracis in relation to epidemiological features, risk factors, bacteriology, x-ray add newer observations in this field which will be useful in diagnosis of these cases
- This study will help to find out the common etiological agent which varies over period and over institutions
- Complications are found to be still common and the data on this and risk factors for complications are lacking which prompted us to go for this study.

SUBJECTS AND METHODS

Methodology

1. Study design : Case Control Study
2. Place of study : ICH
3. Period of study: January 2011 to October 2012
4. Study population

CASE DEFINITION:

Children aged 1month -12 years with clinical, radiological evidence of pleural fluid and conformed by presence of frank pus on thoracentesis.

INCLUSION CRITERIA :

All the children in the age group of 1 month to 12 years who satisfy the case definition will be included in the study

EXCLUSION CRITERIA :

Care givers who does not give consent to participate in the study

SAMPLE SIZE:

All consecutive cases of ET got admitted during the study period were included.

ETHICS:

IRB Approval from Madras Medical College and Written informed consent from the parents were obtained.

MANEUVER

Procedure

- Children aged 1 month to 12 years admitted with history, signs and symptoms consistent with empyema thoracis as per case definition were included in the study.
- Detailed history including age, sex, diet intake, demographic features and clinical features will be elicited and thorough clinical examination was done and entered into the data sheet (Annexure II).
- In all the cases basic investigations including CBC,RFT, LFT with serum protein,CRP,ESR,chest radiography, USGchest, Mantoux, pleural fluid analysis gramstain, AFB screening, bacterial cultures)and blood cultures were done.
- CT chest with contrast were carried out in cases with clinical and radiological suspicion of multiple loculated empyema or non improvement following therapy
- Antibiotics were started in all cases depending upon suspected etiological agent. Antibiotic were changed appropriately based on pus c/s or blood cultures reports subsequently.

- Inter costal tube drainage done with an appropriate sized mallecot tube with an under water seal placed in most dependent position, at point of maximum dullness on percussion as per standard protocols.(annexure)
- ICD was kept insitu till drainage is less than 30-50ml/d and cavity is less than 50 ml in size. Cases that showed definite multi septation, BPF or non improvement with this treatment were subjected to thoracotomy / decortication surgery.
- Patients discharged after clinical recovery with oral antibiotics → follow up as advised at one and three months.

Definition for recovery :

Total clearance of pus with satisfactory lung expansion necessitating removal of ICD tube.

Definitions of complications

- Prolonged draining of pus: more than 1 week
- Bacteremia: bacteria grown in blood culture
- Unsatisfactory lung expansion with or without significant pleural fluid

- Pleural thickening/ Pleural fibrosis: a peel of uniform thickness surrounds the lung may be associated with calcification / not → X-ray/CT scan finding
- Scoliosis with concavity towards same side of the disease:
- Thoracotomy/decortication/lobectomy.
- Necrotizing pneumonia needing pneumonectomy:
- Bronchopleural fistula
- Death

Definitions for risk factors

- Undernutrition: Protein Energy Malnutrition-IAP classification
- Infants and children less than 3 years were considered at risk for complications/death;
- Lower socio economic class: class IV, class V – (Kuppusami scale)
- Bad child rearing practice: Nasal blowing / oil instillation
- Periodontal diseases /poor orodental hygiene: dental carries /gingival ulcers.
- Mental retardation / cerebral palsy:
- Low birth weight

- Immuno suppressive therapy : steroid therapy
- Past history of measles :
- Recurrent history of LRI /abscesses/hospitalization.
- Interval between onset of the disease and admission to the hospital -> 1 week
- Exposure to antibiotics started outside prior to admission.
- Anemia – hemoglobin < 10 gms /dL
- Hypoalbuminemia- serum albumin < 2.5 gms/dL
- Persistently High ESR,CRP +ve
- USG- Chest: showing multiple septations/loculation
- CT chest: showing underlying parenchymal disease, air fluid level.

Statistical analysis

Descriptive statistics of proportions, mean ±standard deviation were arrived at wherever applicable.

To identify the relationship between each of the factor given in the column with Empyema thoracis, we used the Chi-Square independence test. The null and alternate hypothesis is given below.

H0 (Null): The variable in the column in independent of Empyema

H1 (Alternate): The variable in the column in dependent of Empyema

If p-value is less than 0.05, we reject the null hypothesis that is the factor given in the column is highly dependent (correlated) with the outcome of Empyema.

To associate between risk factors and complications Odds Ratio with 95% confidence interval [OR (95% CI)] were arrived at by univarite analysis.

To adjust for the confounders, adjusted [OR (95%CI)] will be arrived at by multivarite analysis.

P<0.05% will be considered for statistical significance

To identify the significant factors that affect "Complication" and "non complication" in patients with empyema thoracis we used the methodology logistic regression. Logistic regression is a type of regression analysis used for predicting the outcome of a binary (in our study complication vs. non complication) dependent variable based on one or more predictor variables. The significant variables can be identified with any p-value less than 0.05.

OBSERVATIONS AND RESULTS

Total number of patients admitted in our		
Hospital during the study period	-	65056
Total number of empyema thoracis		
Patients during the study period	-	90
Number of children who recovered		
Without complications	-	26 (control)
Number of children who recovered		
With complications	-	56
Death	-	8
		64 (cases)

Table 2: Hospital Admission of Pneumonia and Empyema thoracis

Year	Total Hospital Admission n (%)	Pneumonia cases n (%)	Empyema Thoracis n (%)
Jan 2011 – Dec 2011	35052	148(0.4%)	53(0.15%)
Jan 2012 – Oct -2012	30004	112(0.37%)	37(0.12%)
Total	65056	260(0.39%)	90(0.138%)

Table 3: Complications of empyema thoracis

Complications	Count	%
No complication	26	29%
Death	8	8.89%
Decortication	43	47.78%
Pl.Fibrosis	0	0.00%
Thickening	11	12.22%
BPF	2	2.22%
Scoliosis	0	0.00%

Of the total 90 consecutive cases of empyema thoracis, 26 patients (29%) recovered without complications and 64 patients (71%) had complications. Eight (8.89%) patients died. There was a need for decortication in 43(47.78%) patients, pleural thickening occurred in 11 (12.22%) patients and bronchopleural fistula occurred in 2 (2.22%) patients. There were no scoliosis and pleural fibrosis.

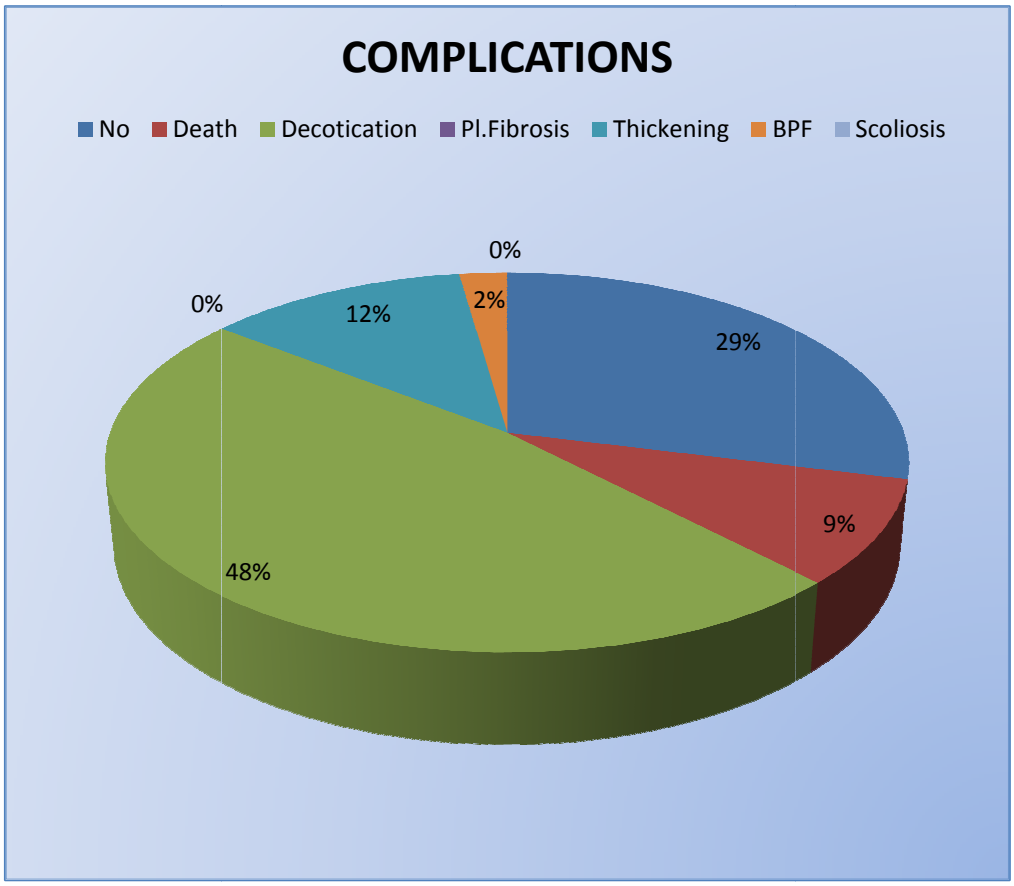

Fig.1. Complications on Empyema Thoracis

Table 4: Correlation of complications to age in cases of empyema thoracis:

Factor Influencing Complication		
Age Group:	**No Complication**	**Complication**
<= 12 Months	13 (50%)	24 (38%)
1 - 3 Years	8 (31%)	21 (33%)
3 - 8 Years	4 (15%)	14 (22%)
8 - 12 Years	1 (4%)	5 (8%)

P-value =0.03 OR = 7.702

In our study of total 90 children 37(41%) children were less than one year and out of that 13 (50%) improved without complications and 24 (38%) had complications. About 29 (32%) were in the age group between 1-3 years of which 8 (31%) improved without complications and 21 (33%) had complications.18 children was in the age group between 3 – 8 years and of this 4 (15%) patients had no complications and 14 (22%) had complications. About 6 children (7%) were there in the age group between 8 – 12 years and in this 1 (4%) improved without complications and 5 (8%) had no complications.

From the above table it is found that children aged less than one year has a significant higher chance of developing complications than children in other age group (P =0.03).

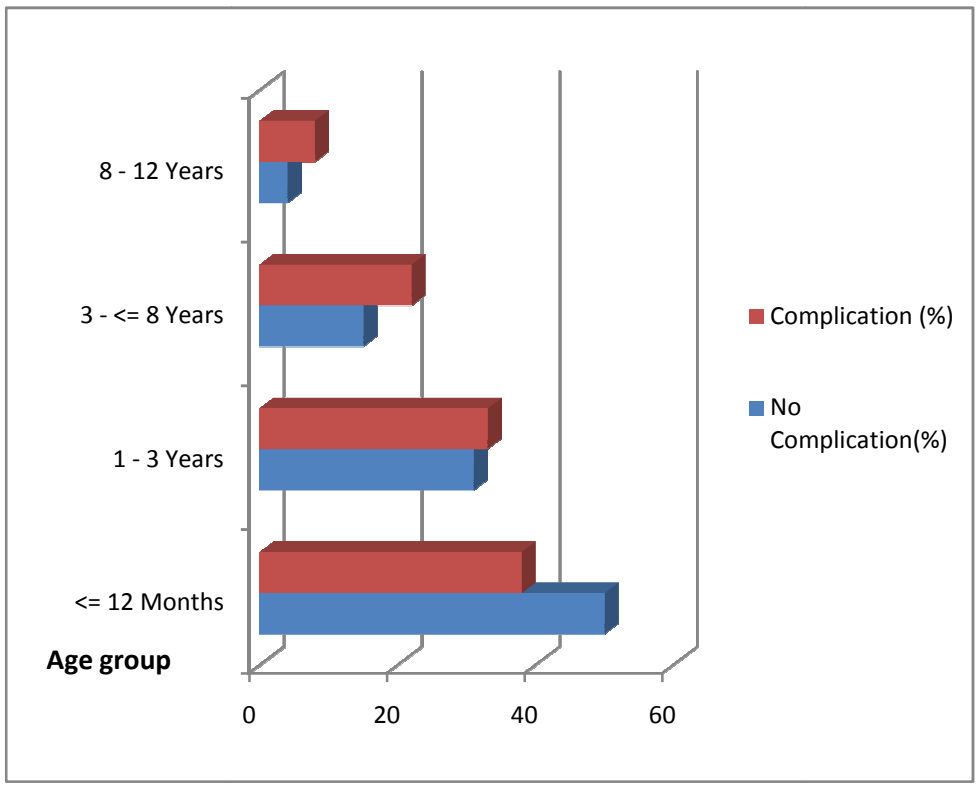

Fig.2 Correlation of complications to age in cases of empyema thoracis

Table 5 : Sex distribution of children with empyema thoracis

Sex	Count	%
Male	50	56%
Female	40	44%

Sex distribution was almost equal with slight male preponderance with ratio of 1.25: 1.

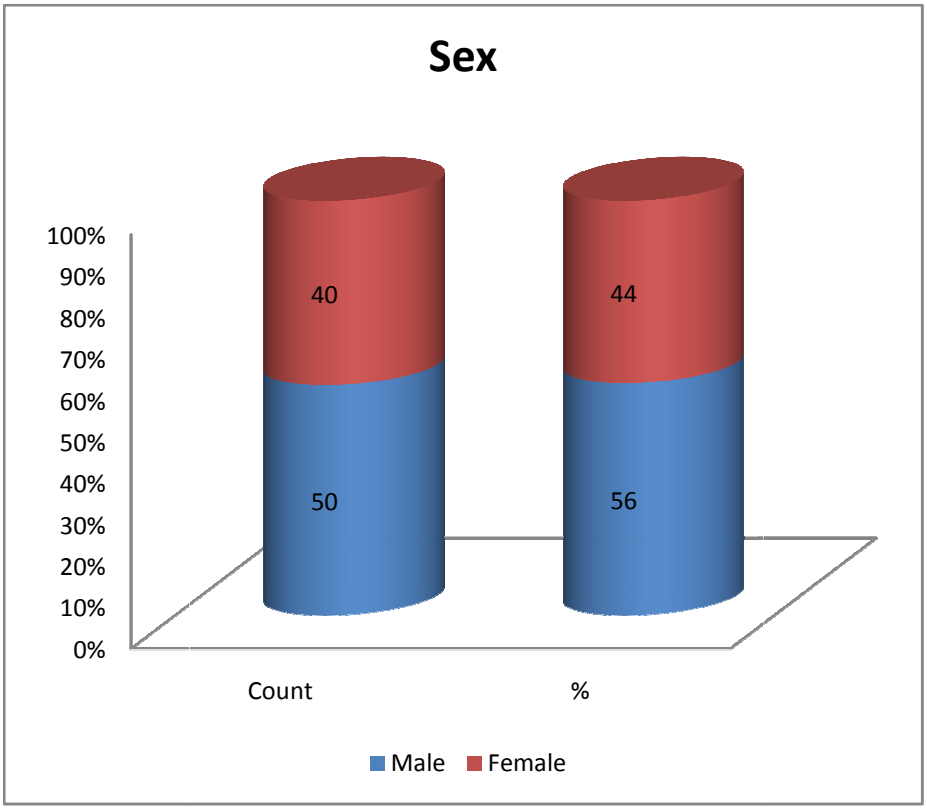

Fig.3 Sex distribution in study population.

Table 6: Presenting symptoms among cases of empyema thoracis

Symptoms	Number	Percentage %
Fever	90	100
Cough	85	94.44
Chest pain	34	37.78
Dyspnoea	75	83.33
Pain abdomen	12	13.33
Altered sensorium	17	18.89
Shock	7	7.78

Almost all children presented with fever as the presenting symptom. Cough was present in 94 %.Chest pain was present in 38%, breathlessness in 83% and abdominal pain in 13%. About 18% presented with altered sensorium and 8% presented with shock.

Table. 7: Socio-economic status versus complications in empyema thoracis

Factor Influencing Complication			Significance
Socio Economic	**No Complication**	**Complication 64 (71%)**	**p - Value**
Upper Middle	0 (0%)	10 (16%)	0.0011
Lower Middle	11 (42%)	18 (28%)	
Upper Lower	13 (50%)	27 (42%)	
Lower Lower	2 (8%)	9 (14%)	

Odds ratio – 0.02.

About 42% of the children with empyema belong to upper lower class in complications group and about 14 % are in lower lower class according to modified Kuppuswami scale (Table).

Table.8: Association of recurrent LRI with empyema thoracis

Factor Influencing Complication			**Significance**
H/O Rec LRI.	**No Complication**	**Complication 64 (71%)**	**p - Value**
Yes	4 (15%)	26 (41%)	0.258
No	22 (85%)	38 (59%)	

History of recurrent lower respiratory tract infection was present in 41 % of the children in those with complication when compared to 15% among those who did not go for complications which was found to be statistically non significant.

In our study about 55% of the children in both the age groups had hospital stay of 2 – 4 weeks. There was no significant difference observed.

Table.9: Hospital stays against complications in empyema thoracis

Factor Influencing Complication		
	No Complication **n = 26 (29%)**	**Complication** **n = 64 (71%)**
Hospital stay		
<= 15 days	10 (38%)	16 (25%)
16 - 30 days	14 (54%)	36 (56%)
> 30 days	2 (8%)	12 (19%)

P value = 0. 3701

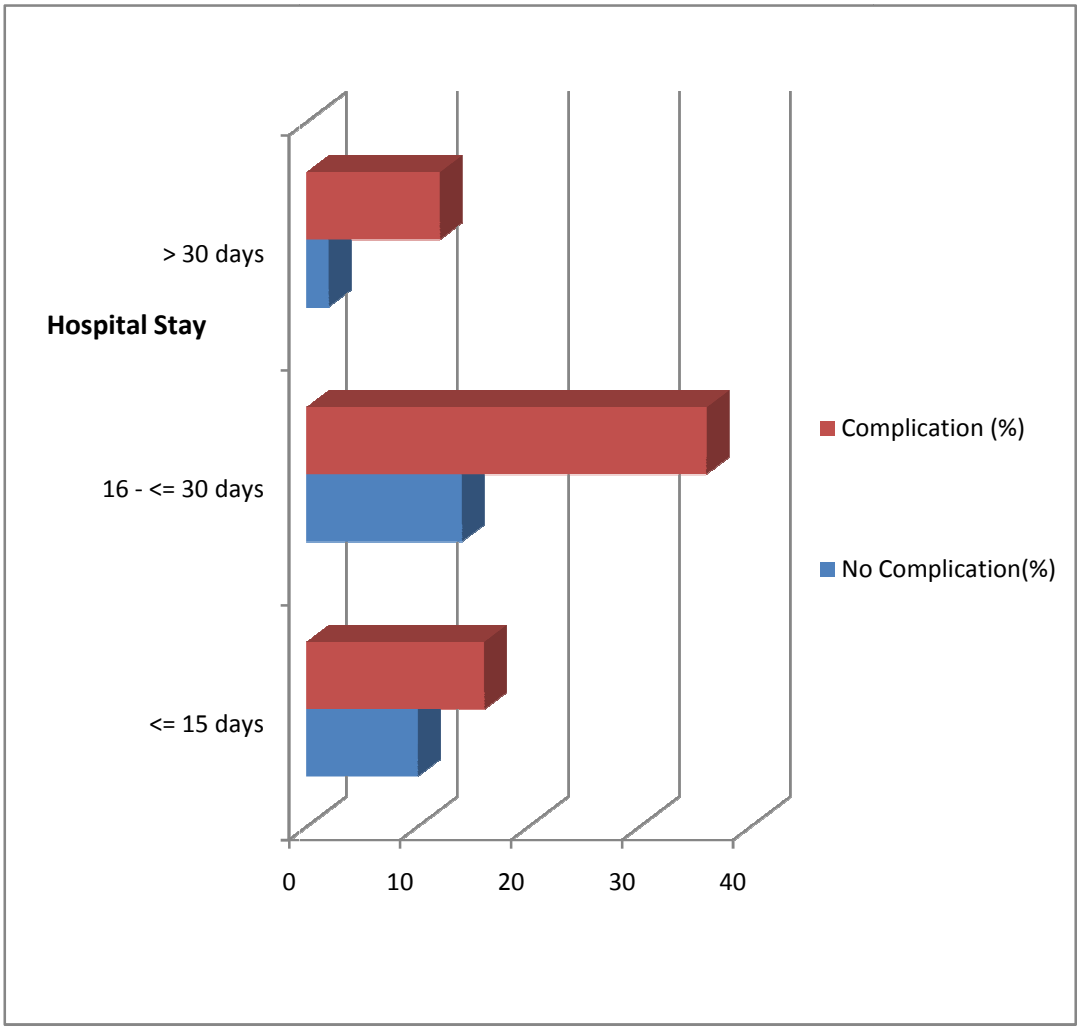

Fig .4 Hospital stays against complications in empyema thoracis

Table 10 : Comparison bad child rearing practices in both groups.

Factor Influencing Complication			**Significance**
Bad CRP	**No Complication**	**Complication**	**p - Value**
	26 (29%)	**64 (71%)**	
Nasal Blowing	4 (15%)	13 (20%)	0.8414
Sambarani Fumes	3 (12%)	3 (5%)	
No	19 (73%)	48 (75%)	

Almost 75 % of the children in both the age group had no history of any bad child rearing practice.

Table 11 : Exposure to prior treatment before admission:

Factor Influencing Complication		
Treatment prior to admission	**No Complication n =26 (29%)**	**Complication n = 64 (71%)**
No	7 (27%)	23 (36%)
Oral AB	16 (62%)	33 (52%)
IV AB	3 (12%)	5 (8%)
ICD Inserted	0	3 (5%)

P-Value: 0.316.

In our study it was found that about 33(52%) children had received oral antibiotics outside before admission to our hospital. About 8 children had intravenous antibiotics before admission and 3 patients were referred with inter costal tube in situ there was no difference among the study groups

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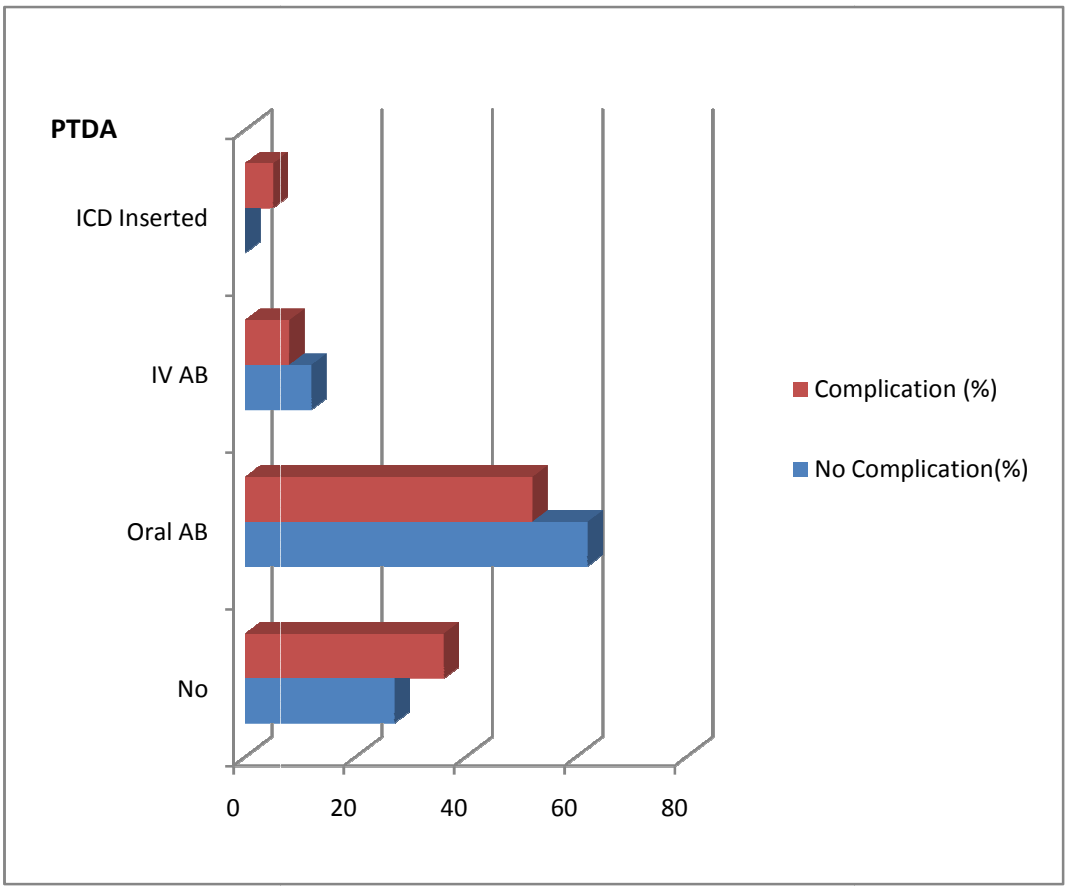

Fig .5 showing distribution of prior hospital therapy

Table 12: Distribution of nutritional status in both groups:

Factor Influencing Complication			**Significance**
W/ A	**No Complication** **26 (29%)**	**Complication** **64 (71%)**	**p - Value**
Normal	14 (54%)	35 (55%)	0.3179
UN	12 (46%)	29 (45%)	

It was found that 45 % of the children with complication were under nourished and 46 % of those who recovered without complications were undernourished. The nutritional status was comparable among the groups

About 25 % of the children in both the group had dental caries. About 13 % in the complication group had tonsillitis. In about 59% the oral cavity was normal in both age groups.

Table 13: Comparison of oral hygiene in both groups:

Factor Influencing Complication			**Significance**
Oral cavity	**No Complication**	**Complication**	**p - Value**
Dental Carries	6 (23%)	16 (25%)	
Oral ulcers	5 (19%)	9 (14%)	0.5844
Tonsillitis	2 (8%)	8 (13%)	
No	13 (50%)	31 (48%)	

Of the total 90 children with empyema thoracis 73(81%) children had hemoglobin less than 10gm/dL. About 54(60%) children had hemoglobin less than 10 gms/dl\L in the complications group.23 (36 %) children had hemoglobin less than 8 gm/dL.

Table 14: Anemia distribution in both groups:

Factor Influencing Complication		
Anemia g/dl	**No Complication** **26 (29%)**	**Complication** **64 (71%)**
More than 10	7 (27%)	10 (16%)
8 - 10	12 (46%)	31 (48%)
6 - 8	4 (15%)	22 (34%)
<6	3 (12%)	1 (2%)

P – Value: 0.295

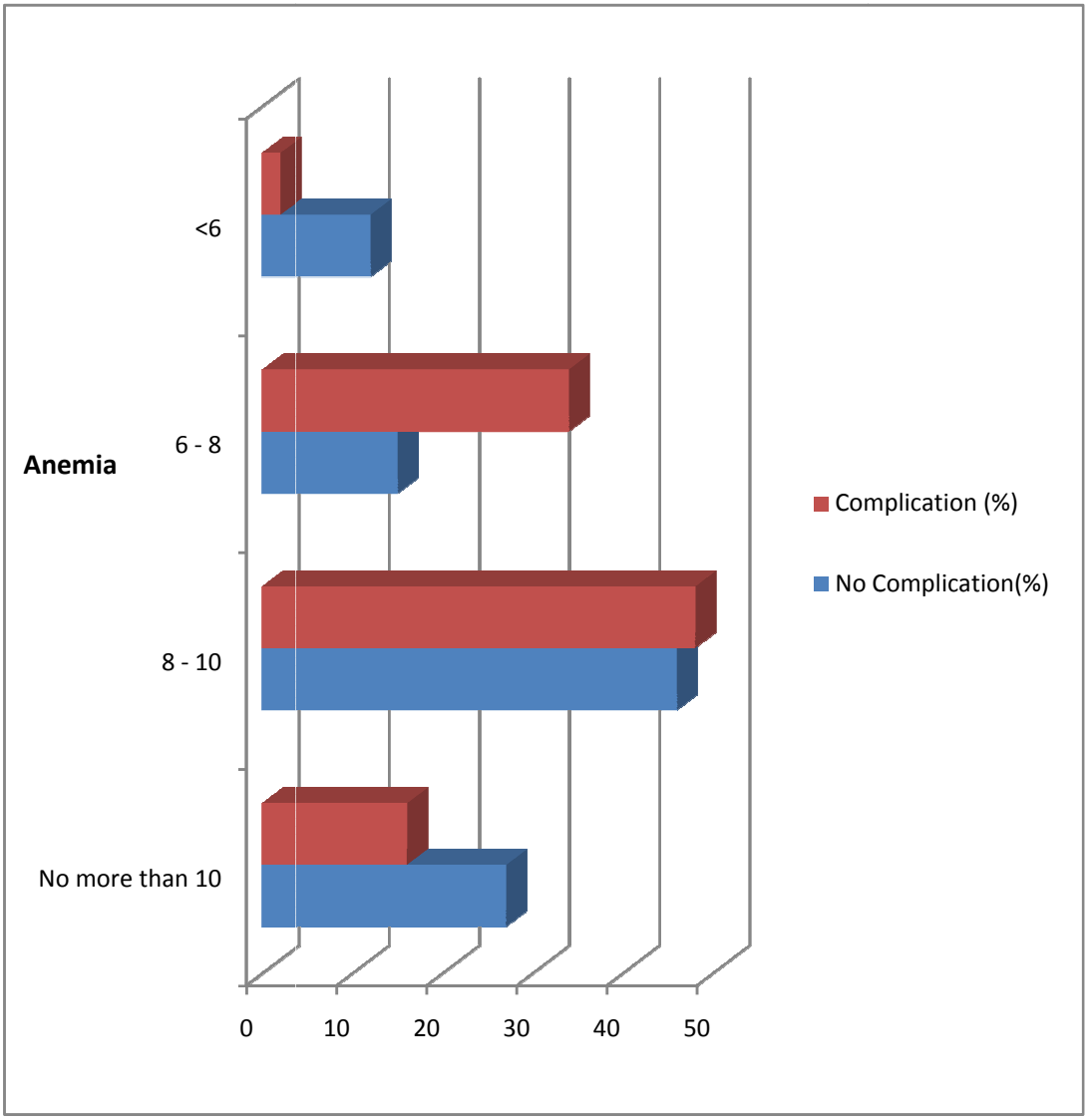

Fig. 6 showing distribution of anemia in both group:

Table 15: Comparison serum albumin values in both groups:

Factor Influencing Complication			**Significance**
Albumin g/dl	**No Complication 26 (29%)**	**Complication 64 (71%)**	**p - Value**
<2.5	11 (42%)	27 (42%)	0.033
>2.5	15 (58%)	37 (58%)	

In our study it was observed that 58% of the children in both the group had albumin levels greater than 2.5. The P-value obtained was significant

Table 16: Comparison of C- reactive protein in both the groups.

Factor Influencing Complication		
CRP	**No complication** **26 (29%)**	**Complication** **64 (71%)**
Positive	25 (96%)	29 (45%)
Negative	0	1 (2%)
Persistently Positive	1 (4%)	34 (53%)

P – Value: 0.0218

Odds ratio -18.397

In all cases C-reactive protein was positive at the beginning and 34 children (53%) had persistently positive C-reactive protein.

Persistently positive C- reactive protein has significantly higher odds of (18.397) in patients having complication of patients with empyema thoracis.

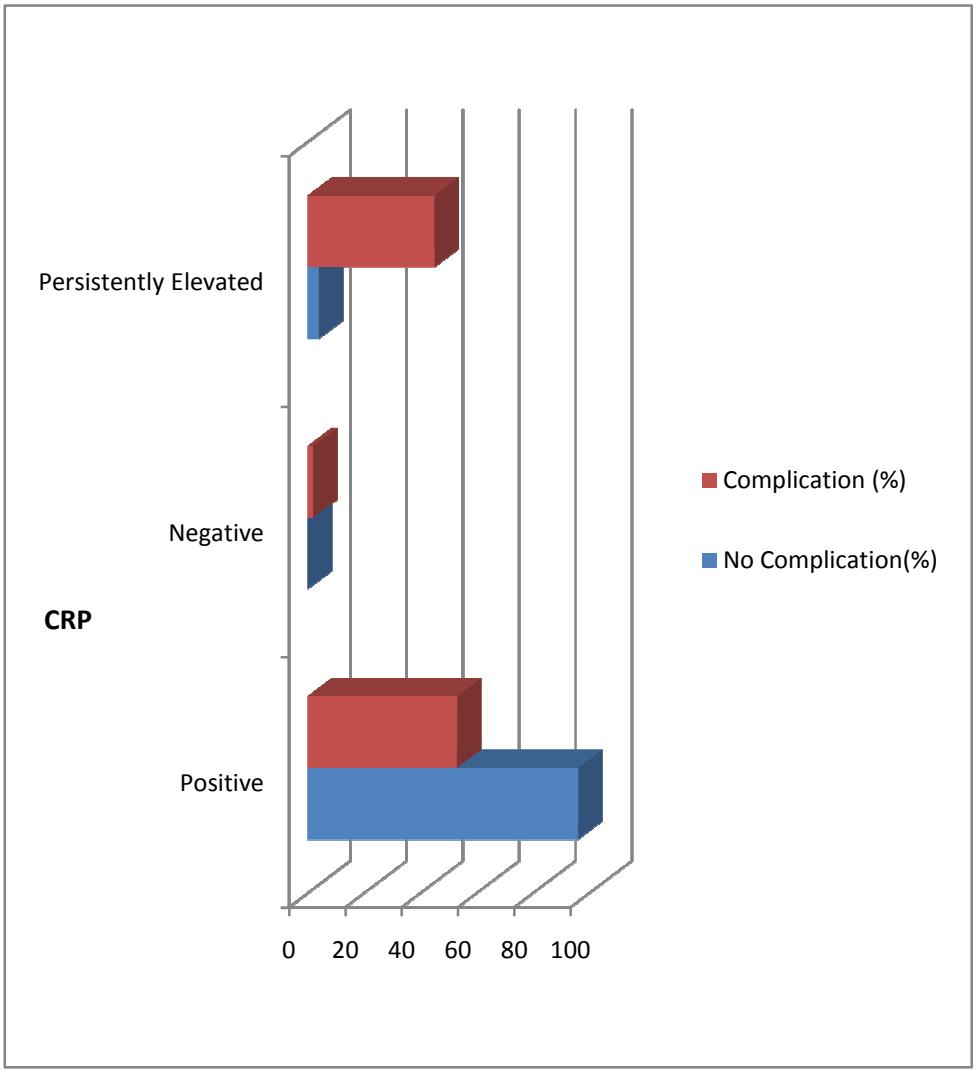

Fig .7 showing distribution of C-reactive protein in both groups.

Table 17 : Comparison of gram stain smears in both the groups.

Factor Influencing Complication			**Significance**
Gram Strain	**No Complication n = 26**	**Complication n = 64**	**p - Value**
GPB	0	2 (3%)	0.0299
GNB	6 (23%)	8 (13%)	
GPC	14 (54%)	22 (34%)	
Negative	6 (23%)	32 (50%)	

Odds ratio – 6.676

About 40% of the children with empyema were positive for Gram positive cocci in Gram stain smear examination. 34 % of the smears were positive for gram positive cocci in complication group.

It was found that Gram positive cocci has significantly higher odds of (6.676) having complications of empyema thoracis.

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Table 18 : Pleural fluid culture yield in both group.

Factor Influencing Complication			**Significance**
C/S	**No Complication** **26 (29%)**	**Complication** **64 (71%)**	**p - Value**
Staph	6 (23%)	18 (28%)	0.9565
GNB	3 (12%)	7 (11%)	
No Growth	17 (65%)	39 (61%)	

Staphylococcus aureus was the commonest organism cultured in both the groups. Almost in 60% of the patients in both groups the results there were no growth from the pus. 11% of the children had Gram negative bacilli grown in their culture (E.coli – 2, Klebsiella – 7, Pseudomonas – 1) (P =0.95).

Table 19 : Comparison of first done chest ultra sonographty in both group.

Factor Influencing Complication			**Significance**
USG 1	**No Complication**	**Complicatio n**	**p - Value**
Multiple Loculation	1 (4%)	21(33%)	0.564
Underlying con+ No loculation	3 (12%)	2 (3%)	
No Loculation	21 (81%)	5 (8%)	
Multi loc + consolidation	1 (4%)	36(56%)	

33 % of the children with complications had multiple loculation at the presentation. About 50 % had multiple loculations with underlying lung consolidation. The difference did not achieve statistical significance.

Table 20 : Comparison of X – ray chest done after inter costal tube insertion.

Factor Influencing Complication		
	No Complication	**Complication 64 (71%)**
X-ray 2		
Nil	0	3 (5%)
Improved	14 (54%)	1 (2%)
Partially Improved	6 (23%)	19 (30%)
Underlying Con	6 (23%)	12 (19%)
Not Improved	0	16 (25%)
PI + UC	0	13 (20%)

P – Value: 0.0568

Odds ratio – 7.256

In 3 patients the second X- ray after inter costal drainage was not taken as they presented with shock and succumbed to disease. About 19(30%) patients had partially improved X-Ray after first ICD insertion.

Odds of patients with partially improved X-Ray after ICD insertion is 7.256 in patients with complications than in patients who improved without complications.

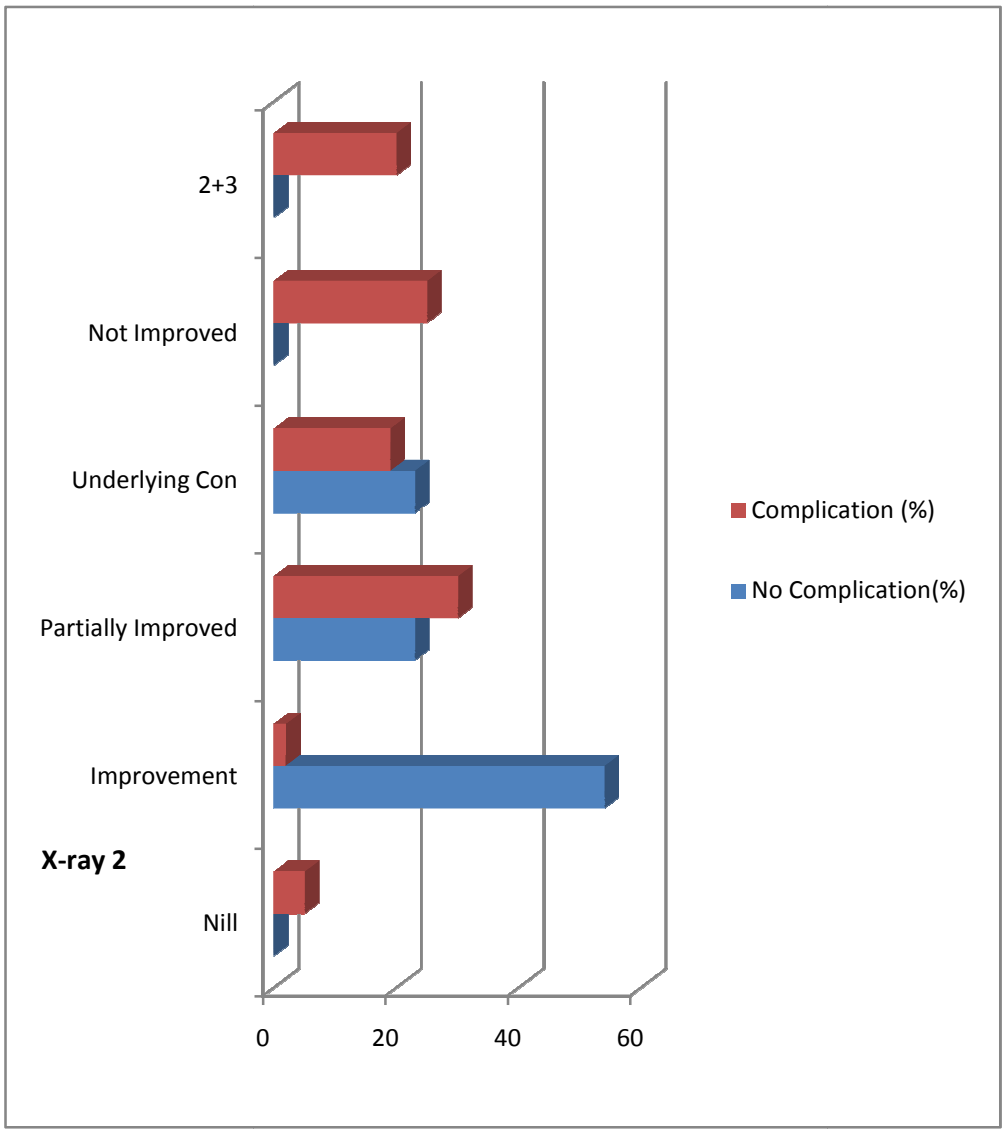

Fig.8 Pictorial representation of chest X- ray taken after chest drain insertion.

Table 21 : Comparison of CT – chest taken in both the groups.

Factor Influencing Complication			**Significance**
C T Scan	**No Complication 26 (29%)**	**Complication 64 (71%)**	**p - Value**
Underlying Con	20 (77%)	4 (6%)	0.0019
ML+Thick pleura+con	2 (8%)	52 (81)	
BPF	0	1 (2%)	
Not Done	4 (15%)	7 (11%)	

Odds ratio -18.61.

There was one case of bronchopleural fistula .81 % of the children with complications had multiple loculations with thick pleura and diseased underlying lung, which was prone for complications. CT chest was not done in 12.2% of the children.

Children with multiple loculations with thick pleura and underlying diseased lung has significantly higher odds of (18.61) developing complications than in those who improved without complications.

Table 22 : Comparison of first line antibiotics started in both the groups.

AB I	No complication	With complication	Total
Cef + Ak	10(38.5%)	23(35.93%)	33(36.67%)
Cef+clox	10(38.5%)	10(15.5%)	20(22.22%)
Ceftriaxone	2(7%)	6(9%)	9(9.9%)
Cef+Ak+Metro	4(15%)	24(37.5%)	28(31.11%)

P –Value: 0.0346

OR – 3.457

Cefotaxime and amikacin is the most commonly used antibiotic combination. Cefotaxime and cloxacillin was most commonly used in children without complications than those with complications. Further the combination of cefotaxime, amikacin and metronidazole was used in 37.5 % of the children in complication group which was found to be statistically significant.

Patients started on cefotaxime, amikacin with metronidazole has significantly higher odds (OR - 3.457) of developing complications of empyema thoracis than those who improved without complications.

Table 23 : Distribution of second line antibiotics used in empyema thoracis.

AB II	Count	%
NIL	14	15.56%
Mero	3	3.33%
Piptaz	1	1.11%
Vanco	68	75.56%
CD	0	0.00%
Metro	3	3.33%
Total	89	98.88%

Vancomycin was the most commonly used second line drug (75.56%)

Table 24 : Comparison of duration of antibiotics in both age group.

Factor Influencing Complication			**Significance**
IV AB duration	**No Complication 26 (29%)**	**Complication 64 (71%)**	**p - Value**
2 weeks	10 (38%)	4 (6%)	0.036
2 - 4 weeks	11 (42%)	26 (41%)	
> 4 weeks	5 (19%)	34 (53%)	

Odds ratio - 43.286.

34 patients (53%) in the complication group had more than four weeks of intravenous antibiotics .Only 19% in no complication group needed intravenous antibiotics for more than four weeks.

Patients who had complications were 43 times most likely would need antibiotics (symptomatic with fever) when compared to those without complications.

Table 25 : Comparison of duration of chest tube drainage on both the groups.

Factor Influencing Complication			**Significance**
ICD	**No Complication** **26 (29%)**	**Complication** **64 (71%)**	**p - Value**
<1 week	5 (19%)	7 (11%)	0.2854
1 - 2 week	17 (65%)	36 (56%)	
2 - 3 week	4 (15%)	21 (33%)	

36 children (56%) had inter costal tube insitu for 2 weeks in the complications group and about 33 % had ICD insitu for 2 – 3 weeks. P – Value was not significant.

Table 26 : Factors influencing pleural fluid culture in empyema thoracis.

Factor Influencing Empyema				**Significance**
	Staph (27%)	**GNB (11%)**	**No Growth (62%)**	**P - Value**
Sex:				0.2514
Male	13 (54%)	8 (80%)	29 (52%)	
Female	11 (46%)	2 (20%)	27 (48%)	
Age Group:				0.7231
<= 12 Months	10 (42%)	4 (40%)	23 (41%)	
1 - 3 Years	10 (42%)	4 (40%)	15 (27%)	
3 - <= 8 Years	3 (13%)	2 (20%)	13 (23%)	
8 - 12 Years	1 (4%)	0	5 (9%)	
Socioeconomic				0.1068
Upper Middle	4 (17%)	2 (20%)	4 (7%)	
Lower Middle	7 (29%)	1 (10%)	21 (38%)	
Upper Lower	12 (50%)	7 (70%)	21 (38%)	
Lower Lower	1 (4%)	0	10 (18%)	

Table 27 : Factors influencing pleural fluid culture in empyema thoracis.

Factor Influencing Empyema				**Significance**
	Staph (27%)	**GNB (11%)**	**No Growth (62%)**	**P - Value**
Vaccine				0.2501
Up to age	11(46%)	7 (70%)	41 (73%)	
Not up to age	10 (42%)	2 (20%)	14 (25%)	
Unimmunized	1 (4%)	1 (10%)	1 (2%)	
Not known	2 (8%)	0	0	
Hospital Stay				0.1932
<= 15 days	3 (13%)	2 (20%)	21 (38%)	
16 - <= 30 days	16 (67%)	7 (70%)	27 (48%)	
> 30 days	5 (21%)	1 (10%)	8 (14%)	
Birth Weight				0.726
Normal	19 (79%)	8 (80%)	38 (68%)	
LBW	5 (21%)	2 (20%)	18 (32%)	

Table 28 : Influence of gram stain examination on culture.

Factor Influencing Empyema				**Significance**
	Staph (27%)	**GNB (11%)**	**No Growth (62%)**	**P - Value**
Gram strain (GS)				<0.0001
GPB	0	0	2 (4%)	
GNB	0	7 (70%)	7 (13%)	
GPC	23	0	13 (23%)	
Negative	1 (4%)	3 (30%)	34 (61%)	

By applying chi-square test to the above variables it is found that only Gram stain smear examination results correlates well with the outcome of empyema thoracis.(p- value < 0.001).

Table 29 : Predictors of complications in empyema thoracis.

Significant Factors		
Variables	**P- Value**	**Odds Ratio**
Age Group	0.03	7.702
Economic	0.0257	0.02
Albumin	0.033	0.001
CRP	0.0218	18.397
Gram strain	0.0299	6.676
CT	0.0407	18.61
AB_dur	0.036	43.286
X - Ray2	0.0568	7.256
AB - I	0.0346	3.457

95 % Confidence Interval

From the Logistic Regression model we identified seven significant factors such as Age Group, CRP, Gram Strain, CT scan, X-ray and prior antibiotic duration and first line antibiotic used.

DISCUSSION

Incidence of community acquired pneumonia admitted in our hospital during the study period was 0.39% and incidence of empyema thoracis admitted was 0.138% among the total children admitted during the study period. Empyema thoracis is a increasingly recognized complication of ongoing and uncontrolled pulmonary sepsis or pneumonia in pediatric age group. Pleural effusion is usually secondary to bacterial pneumonia which progresses to empyema thoracis due to many predisposing factors such as malnutrition, immunodeficiency, delay in initiation or irregular treatment and disappearances of signs and symptoms of pneumonia in immunosupressed.(1)

This study was conducted at a tertiary hospital where cases are referred from various district headquarters hospitals. The optimal management of empyema thoracis in pediatric age group is controversial and currently there are insufficient evidences to give a clear guidance for therapy of parapneumonic effusion and Empyema. British Thoracic Society came out with guidelines for management of empyema in 2005(1).

This study was mainly done to find out the causative organism which was more common in our setup and to find out the various factors which are associated with bad outcome in empyema thoracis. Totally 90 consecutive patients diagnosed as empyema thoracis based on aspiration of pus from the pleural cavity were included in the study in the age group between 1 month and 12 years of age admitted in our hospital . 41% of the children were less than one year of age and 73.3% of the children were less than three years of age and this is in accordance with the studies by S.K.Sathpathy, et al and Muhammed Salim, et al (6, 10). This could be because larger percentage of older children might have received antibiotics before diagnosis of empyema and the antibiotics might have partially suppressed the infection for sometime but insufficient to prevent disease and complication .There were no great difference in prevalence of disease between male and female with slight male preponderance of 1.25:1. This is similar study by Muhammed Salim, et al(10).

About 42% of the children with empyema belong to upper lower class in complications group and about 14 % are in lower lower class according to modified Kuppuswami scale which was statically significant with p value = 0.001. This could be probably because most

of the children who came to our hospital are from lower socio economic class.

All the children presented with fever (100%) and cough (94.44%).About 83% had breathlessness, 13% had abdominal pain probably due to lower lobe involvement. 7% of the children presented with shock and about 19% presented with altered level of consciousness.

The period of hospital stay was longer in those patients with complications; about 75% of the patients staying for more than 2 weeks and 19% staying for more than 4 weeks. Further, out of the total 8 deaths 6 child died within 15 days of hospitalization and 3 died within 48 hours of hospitalization due to refractory shock and respiratory failure and needed ICU care .This finding is in contradictory with the study of Sathish, et al who described 14 children's receiving conservative treatment at a secondary level pediatric centre, the median duration of hospital stay was 14 days and no child needed surgical decortications. With this observation the author concluded saying surgical intervention is not needed to prevent long term respiratory complications but the prolonged hospital stay in

the conservative group had significant health economic implications (19).

History of recurrent lower respiratory tract infection was present in 41 % of the children in those with complication which was found to be statistically nonsignificant. (P value >0.05).In our study it was found that about 33 children (52%) had received oral antibiotics outside before admission to our hospital. Eight children had intravenous antibiotics before admission and 3 patients were referred with inter costal tube in situ. This factor was equally distributed in both the groups and the p value was not found to be significant. Most of the cases received in our hospital are those referred with complications and would have received some form of antibiotics either parental or oral. This could be the reason for most of the cultures being negative and the proportion of the cases with complications in our study being high when compared to previous studies.

The microbiological profile of empyema thoracis has changed over times with the advent of newer antibiotics and usage of conjugated vaccines against pneumococcus and H.influenza type-b .About 40% of the children with empyema was positive for gram

positive cocci in gram stain smear examination. 34 % of the smear was positive for gram positive cocci in group with complications. It was found that odds being Gram positive cocci are 6.676 in patients having complications of empyema thoracis when compared to those did not go for any complication.

In our study about 62% of the children had no growth in the pleural fluid culture and staphylococcus aureus was the commonest organism grown(27%), followed by Gram negative bacilli (11%) of which 2 patients had E-coli grown in culture ,6 had Klebsiella pneumoniae grown and 1 was Pseudomonas . The yield of the pleural fluid culture was 29% which is similar to other studies.(6, 8). The lesser yield of culture could be due to the prior use of both oral and parental antibiotics before admission and another cause could be late referral of cases from other institutions. In our hospital the pus sent to the microbiology department were streaked in both chocolate agar and maconeky agar for the growth of both Gram positive and Gram negative organisms. Anaerobic cultures are not done and latex agglutination test for capsulated organisms like Pnemococcus and H.infleenza type b were not done which could have been yet another reason for poor positivity rate of etiological agents in our study.

In previous studies it was found that malnutrition was associated with complications of pneumonia like going for parapneumonic effusion and empyema thoracis(1).In our study we found that 55% children were nutritionally normal and were equally distributed in both groups . Anemia was not found as a significant factor that affects outcome in patients with empyema thoracis.

Albumin levels are lower in children with empyema. In our study of the total 90 children 42 % of the children had albumin levels less than 2.5 g/dl in both the groups. In this 27 children who had albumin level less than 2.5 g/dl, 5 children had values less than 2 g/dl.

Previous studies done showed that acute phase reactants like total neutrophil count, total WBC count, erythrocytes sedimentation rate, C-reactive protein and procalcitonin were not able to differentiate between viral and bacterial etiology (22, 23) .Embiya Dilber, et al (28) in a study found CRP proved useful in predicting complications and it is a sensitive marker not only for diagnosis but also for follow up of treatment outcomes. In our study, we found that in all cases C-reactive protein was positive at the beginning and 34(53%) children had persistently positive C-reactive protein. Persistently positive

C- reactive protein was associated with complications of empyema (p-value = 0.0218, OR = 18.397). Further, total WBC count and ESR were not able to predict the outcomes in patients with empyema. In clinical practice serial measurements of both C-reactive protein and total count are found to be useful in the follow up of cases.

Biochemical characteristics of pleural fluid have not be shown to be of any value in management of children with parapneumonic effusion and empyema and hence routine aspiration performed solely for the purpose of biochemical analysis are not followed in the west.

Chest ultrasonography is an important investigation in empyema as it can be used to pickup fluid in the pleural cavity and to differentiate solid from liquid material. It can also find out loculations, fibrin stands and estimate the size of effusion and sometimes consistency of the fluid. Since there is no radiation exposure and a need for sedation, it is one of the preferred investigation in children. It also helps in selecting the site for aspiration of fluid and used as a guide for inserting chest tubes. In our study we found that about 33% in complication group had multiple loculations and 56% had multiple loculations with underlying diseased lungs. First ultrasonogram chest

as a predictor of complication was not found to be statically significant (p-value = 0.05).In the follow up scan most of the children in the complication group had multiple loculations with pleural thickening and the underlying parenchyma could not be visualized. Only few research has been done previously regarding the use of ultrasonography and contrast enhanced CT scan chest in the pediatric empyema thoracis. British thoracis society guidelines for pediatric empyema (2005) recommend not to take CT chest normally in all patients. It has be shown in previous studies (21) in children and in few adult studies that CT chest was not helpful in differentiating parapneumonic effusion from simple or complex empyema nor they were able to predict complications. We found that 81 % of the children with complications had multiple loculations with thick pleura and diseased underlying lung, which was prone for complications. CT chest was not done in 12.2% of the children.

Children with multiple loculations with thick pleura and underlying diseased lung are prone for developing complications than in those who improved without complications (OR -18.61). In our setup CECT chest are usually taken when children have signs of loculations on chest ultrasonography and poor drainage of pus in spite

of broad spectrum antibiotics and need for repeated chest tube insertions. The thickened pleura in empyema take the contrast and split pleura sign can be demonstrated on CECT chest. In most of the times CT chest is taken pre-operatively to access the underlying lung.

The findings seen in the X –ray taken after the ICD insertion correlated well with the complications of empyema. About 30% had partial improvement on the second X-ray (P-Value: 0.051. OR – 7.256), 25 % had no improvement and 20% had partial improvement and underlying lung consolidation. In our hospital, fibrinolytics are not used as a treatment option in addition to antibiotics and chest tube drainage. Fibrinolytics like streptokinase and urokinase lyse the fibrinous strands in loculated empyema thoracis and thereby clear the lymphatic pores. This breaks the adhesions in the pleural space and in turn increases drainage of pleural fluid or pus reducing the septic load. Probably this could explain the partial improvement of the second X-ray in the complication group.

Review of previous studies (16,18,19) showed that on a overall about 60 – 80 % of the children could be managed with chest tube and antibiotics alone , The concept of fibrinolytics instillation and early

thoracoscopic surgery came in mid 1990s (2). Coming to the first line antibiotics instituted in our hospital in about 37 % of the children cefotaxime with amikacin was distributed almost equally in both the groups. Cefotaxime with cloxacillin was used more commonly in the no complication group than in the group with complication. Further the combination of cefotaxime, amikacin and metronidazole was used in 37.5 % of the children in complication group which was found to be statistically significant.

Patients started on cefotaxime, amikacin with metronidazole has significantly higher odds (OR - 3.457) of developing complications of empyema thoracis than those who improved without complications. Since Staphylococcus aureus was the most common organism isolated in our setup probably adding a antistaphylococcal antibiotic like cloxacillin might improve the treatment outcome.

Vancomycin is used as a second line drug in 68% of the children and only 14 % of the children settled with first line antibiotics. About 29% of the children were treated with third line antibiotics. On an average about 41 % of the children needed intra venous antibiotics between 2 – 4 weeks and about 53 % of the children in complication

group needed IV antibiotics for more than four weeks in the complication group. In our study about 71 % of the children had complications which is very high when compared to the previous studies (16, 18, 19) which may be probably because of late referral from other institutions or prior exposure to antibiotics temporarily masking the clinical condition.In our hospital chest tubes are generally inserted after seeing evidence of fluid in chest X- ray and after aspiration of pus from the pleural cavity. In many cases Chest ultrasonography is usually done after chest tube insertion .Further fibrinolytics are not used in our setup. It has been well documented in previous studies that use of fibrinolytics reduces the need for surgery except for few complications of the drugs like anaphylaxis and hemorrhage.

CONCLUSION

Out of 90 consecutive cases of empyema thoracis admitted in our hospital 26 children improved without complications and 64 children had complications like death (8.89%), thoracotomy with decortications (47.78%),pleural thickening (12.22%),broncho pleural fistula (2.22%) and no cases had pleural fibrosis, and scoliosis.

Staphylococcus aureus was the most common organism isolated in culture. Presence of gram positive cocci in gram stain was associated with isolation of staphylococcus aureus in pleural fluid culture. Further presence of gram positive cocci in gram stain were associated with worse outcome in empyema thoracis.

Children less than one year are more prone for complications than other age group and there was no specific sex predisposition. Most of the children were from Upper lower class of modified Kuppuswami scale and occurrences of complications were not significantly linked with history of recurrent lower respiratory infection.

Hospital stays in most children were between 16 – 30 days and those with complications stayed for more than 30 days. Persistently positive C- reactive protein was associated with complications

Presence of multiple loculations with underlying diseased lung was found in 56 % of those with complications, but was not found statistically significant.Presense of partial improvement or no improvement in the chest x-ray taken after chest tube insertion was associated with complications of empyema thoracis.

Presence of multiple loculations with underlying lung consolidation in CECT chest with contrast enhancement and thick pleura was associated with poor treatment outcome.

Those children who had complications of empyema thoracis needed intravenous antibiotics for more than four weeks than children who improved without complications.

Further use cefotaxime, amikacin with metronidazole was associated more with complications and usage of antistaphylococcal antibiotic like cloxacillin was associated with improved outcome.

LIMITATIONS OF THE STUDY

- The sample size was small to make comparisons and to draw conclusions for the general population.
- The control group that is children without complications was small in number when compared to the cases that is children with complications.
- Study was conducted in a tertiary pediatric institute were cases are referred from other hospitals mostly with complications, so this population does not match with general population.
- Anaerobic cultures were not carried out in our institution and latex agglutination for pneumococcus was not carried out.
- Time of surgical referral was not uniform in all cases.

RECOMMENDATIONS

- Well controlled studies with more study sample with age matched controls are needed to confirm these findings.
- Chest ultrasonography should be done prior to chest tube placement and if possible chest tubes should be placed under sonographic guidance.
- Fibrinolytic therapy as a treatment option should be added to the current management to improve pus drainage.
- Anti staphylococcal antibiotic to be added as a first line antibiotic in children with suspected empyema thoracis.

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ETIOLOGY, OUTCOME AND RISK FACTORS FOR EMPYEMA THORACIS IN CHILDREN AGED 1 MONTH – 12 YEARS IN A TERTIARY CARE CENTRE

1.	**Patient name (in Caps)**	**Sex** 1. Male ☐ 2. Female ☐
2.	**Age**	YY ☐☐ MM ☐☐
3.	**Date of admission** ☐☐ ☐☐ ☐☐	**Date of discharge** ☐☐ ☐☐ ☐☐ **Date of surgery** ☐☐ ☐☐ ☐☐
4.	**Father's Name**	**Qualification** : 1. Illiterate 2 .Primary (≤ grade 5) 3. Secondary (grade 5-12) 4. Graduate Occupation: 1. Unemployed 2. Unskilled labour 3. Skilled labour 4. Business 5. Professional 6. Others
5	**Mother's Name**	**Qualification** : 1. Illiterate 2.Primary (≤ grade 5) 3. Secondary (grade 5-12) 4. Graduate ☐ Occupation: 1. Unemployed 2. Unskilled labour 3. Skilled labour 4. Business 5. Professional 6. Others ☐
6.	**Residence**	1. Chennai Corporation 2. Others ☐
7.	**Address** **Door No:** **Street :**	WD/Town State: Pin Code: ☐☐☐☐☐☐
8.	**Socio Economic Class Modified Kuppyswamy scale**	Specify--

CLINICAL HISTORY

9.	**Fever**		1. Yes ☐ 2. No ☐
	a.	If Yes	Duration
	b.	Amplitude	1.Low 2. Moderate 3. High
	c	Periodicity	1.Continuous 2. Intermittent 3. Remittent
	d.	Chillis	1. Yes 2. No ☐
10.	**Cough & Cold**		1.Yes ☐ 2. No ☐ Duration-----

11.	**H/O Breathlesness**	1.Yes ☐ 2. No ☐ Duration
12.	**H/O Cyanosis**	1.Yes ☐ 2. No ☐ Duration
13.	**H/O Chest retractions**	1.Yes ☐ 2. No ☐ Duration
14.	H/O Noisy Breathing	1.Yes ☐ 2. No ☐ Duration
15.	Refusal of feeds	1.Yes ☐ 2. No ☐ Duration
16.	H/O bad CRP	1.Yes ☐ 2. No ☐ If yes Specify a.Nasal blowing b.Oil instillation c.Sambrani fumes d.Others
17.	Skin Infections	1.Yes ☐ 2. No ☐
18.	Ear discharge	1.Yes ☐ 2. No ☐
19.	H/O Poor oro-dental Hygiene	1.Yes ☐ 2. No ☐ If yes Specify a.Dental caries b.Ginguval Ulcers c.Oral Ulcers d.Others
21.	H/O Passing worms	1.Yes ☐ 2. No ☐
22.	**H/O of Vomiting**	1.Yes ☐ 2. No ☐ Duration
23.	**Others Specify**	
24.	**Immunisation** **a. National immunization schedule**	1. Up to Age 2. Not upto age 3. Unimmunized 4. Not known
	b. Others Specify	

PAST HISTORY

25.	**H/O Measles**	**When –** **Treatment details**
26.	H/O Recurrent skin abcesses/infections	**No. of episodes/year-**

27.	H/O Recurrent RTI	1.Yes ☐ 2. No ☐ If Yes---- URI / LRI No.of episodes /year----- Treatment details
28.	H/O of Hospitalisation	1.Yes ☐ 2. No ☐ Duration ---- Diagnosis
29.	H/O of seizures	1.Yes ☐ 2. No ☐ If Yes , No.of episodes /year---- Treatment details
30.	Developmental delay	1.Present 2.Absent

TREATMENT HISTORY

31.	**X-ray chest taken**	X-ray report – 1. 2.
32.	Pleural Fluid Analysis a. Apperance, b. Grams stain c. C/S	1.Yes 2. No If yes Specify
33.	**Inter costal drain insertion**	1. Yes ☐ 2. No ☐ If Yes 1. Date of insertion 2. Pus(Drained /Not Drained)
34.	Antibiotics	1.Date of starting – 2.Antibiotic used – 3.Duration

EXAMINATION

35.	**Weight -**	Height -
36.	**Sensorium**	1. Normal 2. Altered
37.	**Nutritional status (specify)**	
38.	**Lymphadenitis**	1. Generalizedl 2. Localized Groups involved— Size of the nodes— Matted/Not matted
39.	**Evidence of Tuberclosis**	1. Phlycten 2. Scrofuloderma 3. Healed cervical ulcers
40.	**Oral cavity**	1.Dental carries 2. Gingual Ulcers 3.Oral mucosal Ulcers 4..Angular stomatitis 7.Tonsillits 8.White patches 9.Others

41.	Pulse	Rate-		
42.	Skin infection	1. Yes 2. No		
	If yes describe			
43.	Vitamin deficiency (Specify)	A	B	
44.	BP (mm of Hg)			
45.	RS			
	Respiratory Rate			
	Work of Breathing	1.Grunt 2. Stridor 3.Retractions		
	Tracheal position	1.midline 2.Right 3.Left		
		RIGHT	LEFT	AREAS
	Breath sounds			
	VF			
	VR			
	Percussion			
	If any other findings (specify)			
46.	CVS	1. Normal 2. Abnormal		
	If any findings (specify)			
47.	Abdomen	1. Normal 2. Abnormal		
	If any findings (specify)			
48.	CNS	1. Normal 2. Abnormal		
	If any findings (specify)			

INVESTIGATIONS

50.	**Blood Count**		
	Total Count	Cells/cubic mm	
	Differential Count	P %; L %; E %; M %;	
	Hb %		
	Smear Study Report		
	ESR	1. Half an hour 2. One hour	
51.	**Biochemistry**		
	a. Blood sugar	mgm /dL	
	b. Urea	mgm /dL	
	c. S. Creatinine	mgm /dL	
	d. S. Electrolytes Na	mEq/L	
	K	mEq/L	
	HCO_3	mEq/L	
	e. Total Proteins	mgm /dL	
	f. Albumin	mgm /dL	
	g. Globulin	mgm /dL	
	h.CRP	1 - 2 -	

52.	**MicroBiology**		
	I. Pus		
	a.Gramstain		
	b.AFP stain		
	c. Bacterial culture		
	d. Antibiotic Sensitivity		
	II. RGJ	1. ( )	2.( )
	III. Mantoux test	1. Positive 2. Negative Specify mm.	
	HIV 1 & 2	1. Positive 2. Negative	
	Blood Culture	1. Done 2. Not done	
	If done (Specify organism and Sensitivity)		
	Urine analysis		
	a. Albumin	1. Yes 2. No	
	b. Deposits	1. Yes 2. No	
	If yes Specify		
	d. Others (Specify		
53.	**X ray Chest**	Date	Report
	I		
	II		
54.	**USG - Chest**	Date	Report
	I		
	II		
55.	**CT Chest**	Date	Report
	I		

TREATMENT

56.	**Oral feeds started on**	
57.	**IV fluids**	1. Yes 2. No
	If yes Specify	

58.	Antibiotics		1. Yes 2. No	
	If yes Drug 1		Name:	mg X X days
	Drug 2		Name:	mg X X days
	Drug 3		Name:	mg X X days
	Drug 4		Name:	mg X X days
	Others (Specify)			
59.	ICD Inserted on			
	Days		Drainage	Outcome
	I			
	II			
	III			
	IV			
	V			
	VI			
	VII			
	VIII ICD removed on ---			
60.	Surgeon's opinion			
61.	Any surgical intervention ----- Yes/No If yes Specify Post- op course-			
63.	Diagnosis at Discharge/ Outcome			
64.	Follow up ------- 1st month			
	Symptoms & signs	Fever	Present	Absent
		Breathlessness	Present	Absent
		Chest pain	Present	Absent
		Breath sounds	Equal	Reduced
		ICD site	Healed	Not Healed
		Scoriosis	Present	Absent
	X-ray chest	Lung expansion	Good	fair
		Signs of Volume reduction	Present	Absent
		Scoliosis	Present	Absent
		Report		

ABBREVIATIONS

PPE – Parapneumonic effusion

VATS – Video assisted thoracoscopic surgery

LDH – Lactate dehydrogenase.

ESR – Erythrocyte sedimentation rate.

PCR – Polymerase chain reaction.

CRP – C –Reactive protein.

BPF – Broncho pleural fistula.

CT - Computed Tomography.

GNB – Gram negative bacilli.

GPC - Gram positive cocci.

AFB - Acid fast bacilli.

BTS - British Thoracic Society.

CAP – Community acquired pneumonia.

MASTER CHART

S.No	Sex	Age	HS	SEC	Bad CRP	Vaccine	Measles	H/O Rec. LRI	H/O Rec. Skin infections	Development	H/O Seizures	Birth Weight	PT	W/A	Oral cavity	Anemia	TC	DC	Albumin	CRP	ESR (1 hour)	Gram strain (GS)	AFP	C/S	MX	HIV	Blood culture	X-ray 1	X-ray 2	USG 1	USG 2	CT	A B-I	A B-II	A B-III	AB duration	ICD	Surg opl	Post X-ray	Follow up	complications
1	2	1	1	3	3	1	2	2	2	1	2	1	1	2	5	3	2	2	1	3	2	1	2	3	2	2	2	1	4	2	4	3	1	5	2	2	2	3	0	1	3
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